IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Roderick J. Scott	Art Unit	: 1638
Serial No.	: 10/058,825	Examiner	: Stuart F. Baum
Filed	: January 30, 2002	Conf. No.	: 2437
Title	: METHODS FOR MODIFYING PLANT ENDOSPERM		

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REQUEST FOR REHEARING

Appellants submit this request for rehearing under 37 C.F.R. 41.52. Appellants seek rehearing of the Board's decision of June 4, 2009, wherein the Board affirmed the rejection of claims 20, 21, 62-67, 69, 71, 76-78, and 80-93 under 35 U.S.C. § 112, first paragraph (Written Description), affirmed the rejection of claims 20, 21, 62-82, 85-90, and 93 under 35 U.S.C. § 112, first paragraph (Enablement), reversed the rejection of claims 20, 21, 62-67, 69, 71, 76-78, and 80-93 under 35 U.S.C. § 112, second paragraph, and reversed the rejection of claims 83, 84, 91, and 92 under 35 U.S.C. § 112, first paragraph (Enablement). Rehearing of the matters identified herein is requested because the Board has raised new reasons for the Written Description and Enablement rejections that have not been previously addressed by Appellants, and because the Board has misapprehended or overlooked certain matters of fact or law. Appellants reserve all rights to appeal or other review.

Appellants respectfully traverse the rejections of record and specifically request rehearing by the Board of the points set forth below.

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ARGUMENT

A. Written Description

1. The Board has raised a new ground of rejection in the Written Description decision.

On page 46, lines 1-2 of the Board's decision, the Board states, "Appellant has failed to provide evidence that one of ordinary skill in the art was aware that Met1 is present in the endosperm of any plant type…." This constitutes a new ground of rejection under 37 C.F.R. 41.50(b). Accordingly, Appellants respond by presenting new arguments under 37 C.F.R. 41.52(a)(3).

The expression patterns of Met1 were well known in the art as of the earliest priority date of the present Application. In this instance, the Board overlooked evidence demonstrating that persons of ordinary skill in the art were aware that Met1 is present in plant endosperm. For example, the Finnegan *et al.* publication, which was presented as Appendix D of Appellants' Brief, states: "[m]ost of the known plant methyltransferase transcripts are expressed ubiquitously in vegetative and reproductive tissues....*METI* transcripts are at least 10,000-fold more abundant than those of *METII*." Finnegan *et al.* at page 230. Therefore, as the Board has overlooked specific evidence demonstrating that MET1 transcripts are expressed ubiquitously in vegetative and reproductive tissues, Appellants request the Board withdraw this statement and consider the effect of its withdrawal on the Board's ultimate decision.

Equally important, the demand for evidence of the presence of Met1 in endosperm of any plant suggests that the Board has misapprehended the operation of the claimed invention. In this case, a modified endosperm is the product of removing or attenuating genetic imprinting via demethylation of DNA. As described in Appellants' Specification, inhibiting the production of Met1 in the female germ line produces ovules with hypomethylated DNA. *See e.g.,* page 12, line 28. After fertilization, the differential expression of maternally-inherited alleles results in a modified endosperm and/or embryo. *See e.g.,* Appellants' Specification at page 11 lines 6-10. Appellants specifically employed germline-specific downregulation of Met1 so that the level of Met1 expression in the endosperm of seeds would not be affected. *See, e.g.*, Appellants'

Specification at page 15, lines 22-26. Consequently, Appellants respectfully request that the Board withdraw this statement and consider the impact of its withdrawal on its decision.

2. The Board has overlooked arguments supporting the sufficiency of the Written Description for the methods of claims 63, 69, 76, and 86-93.

The Board has overlooked Appellants' analysis of separately-argued claims 63, 69, 76, and 86-93. Here, the Board erred in stating that, "Appellant attempts to argue claims 63, 64, 67, 69, 76, and 86-93 separately by simply listing their limitations." On pages 25-27 of Appellants' Brief, however, Appellants explicitly incorporated the arguments presented for claims 21, 64, 66, 67, 77, 82, or 83 into the arguments supporting the patentability of claims 63, 69, 76, and 86-93. The Board conceded that the arguments set forth for claims 21, 64-67, 71, 77, 78, and 80-85, 91 and 92 constituted separate arguments under 37 C.F.R. 41.37(c)(1)(vii). *See* Board Decision at pages 46-47. Thus, claims 63, 69, 76, and 86-93 independently stand or fall and Appellants request rehearing as to the adequacy of the Written Description of these claims.

3. The Board has overlooked the U.S.P.T.O.'s Written Description Guidelines and has failed to consider the state-of-the-art of nucleic acid technologies.

On page 44, lines 16 through 20 of the Board's decision, while discussing whether Appellants had provided a sufficient number of species to demonstrate possession of the claimed invention, the Board states that, "the court has since clarified that the complete structure of the representative species does not necessarily have to be described...however, a correlation between the claimed function and structure must be 'known or disclosed.' [*Enzo,* 323 F.3d] at 964 (citing with approval PTO's Guidelines, 66 Fed. Reg. at 1106)." Additionally, on page 47, lines 5-6 of the Board's decision, the Board states that "[Appellants'] Specification does not describe the structures of those members of the genus of partial sequences that act to modify the endosperm of the claimed plants." Here, the Board has overlooked the state-of-the-art for oligonucleotide design and the working examples provided in the Specification.

In articulating the standard of review, the Board failed to acknowledge the March 25, 2008, update to the U.S.P.T.O.'s Guidelines regarding the examination of patent applications under the Written Description requirement of 35 U.S.C. § 112, first paragraph and the particular

impact of the revised Guidelines on the Board's analysis of the claims in the present case. *See* Written Description Training Materials (Revision 1). The March 25, 2008 guidelines were created to supersede and replace the 1999 Training Materials because, "the case law and technology have developed in such a way as to necessitate revision." *Id.* at Preface.

Importantly, the U.S.P.T.O.'s Guidelines demonstrate that one of ordinary skill in the art would have considered the Appellants to have had possession of the entire genus of partial-length oligonucleotides and polynucleotides that can be predicted from the full-length sequences of *Arabidopsis* Met1 and the *Z. mays* Met1 ortholog, having any orientation or length. In this case, Appellants presented evidence that the full-length sequences of the *Arabidopsis* Met1 cDNA and the *Z. mays* Met1 ortholog were well known in the art. *See,* Appellants' Brief at pages 13 and 21, and Appendices B and F. The claims at issue define the structure of partial-length oligonucleotides or polynucleotides: it is a nucleic acid molecule comprising a sequence whose transcription product comprises a partial *Arabidopsis* Met1 (or *Z. mays* Met1 ortholog) sequence. Thus, with knowledge of the full-length sequences, a person of ordinary skill in the art could immediately envision all possible nucleic acid sequences that may be of use in the claimed methods.

Next, as the analysis employed in Example 12 of the updated Guidelines demonstrates, a person of ordinary skill in the art could readily identify the subset of partial-length oligonucleotides and polynucleotides described above that would be effective for downregulating one or more DNA methylating enzymes present in the plant. *Id.* at page 44. First, the partial sequence employed in the working examples described in Appellants' Specification provides at least one additional species beyond the two full-length species discussed above. Second, there are art-recognized correlations between an antisense oligonucleotide's function and the structure of the target mRNA to aid in the selection of fragments having the ability to inhibit translation of a target mRNA. Third, there are also software packages available to assist in predicting partial-length oligonucleotides and polynucleotides that have the claimed activity based on a full-length sequence and the mechanisms by which protein expression can be downregulated. Here, the U.S.P.T.O. explicitly acknowledged that the general knowledge in the art is high—a fact signifying that disclosure of the above-mentioned species is sufficient to convey that the

Appellants were in possession of the entire breadth of the genus of partial-length oligonucleotides and polynucleotides for use in the claimed methods. *See Id.* at page 44.

In addition, the sequences of target nucleic acids in various plants were known as of the earliest priority date, and available to facilitate the design of Met1 oligonucleotides that would have activity in plant types other than *Arabidopsis*. In particular, the Board has overlooked the pre-existing knowledge in the art regarding DNA methytransferases in corn, pea, carrot, and tomato, for example. *See* Appellants' Brief at page 21 and Appendices G, H, and I. These sequences, and other sequences known in the art as of the effective filing date, guide the practice of the invention. Here, the Board has misapprehended the significance of the sequence similarity among the known methyltransferases sequences that has been demonstrated by the Appellants. *See, e.g.,* Reply Brief at page 5, and Appellants' Brief at page 21 and Appendix E. A person of ordinary skill in the art could have readily pictured the essential regions to use in practicing the claimed invention—the regions of high homology.

Moreover, the Board erred by accepting the Examiner's assertion that "the Appellant has failed to provide evidence that one of ordinary skill in the art was aware…that a full or partial antisense sequence to Met1 would result in a modified endosperm." Board decision at page 46. Indeed, the Appellants have demonstrated the production of a modified endosperm using a partial sequence of *Arabidopsis* Met1. Here, the Board has overlooked working examples provided in the Appellants' Specification and the sequence of the Met1 fragment provided in Appellants' Reply Brief (at pages 2-4). Thus, Appellants' Specification provides at least one additional species beyond the two full-length complement species discussed above. Consequently, based on the Specification, the level of skill in the art, and the development of the case law and technology, as embraced by the revised PTO Guidelines, those skilled in the art would conclude that the Appellants were in possession of sufficient representative species of the partial-length oligonucleotides and polynucleotides of claims 20 and 62 for use in the claimed methods at the time of filing.

Indeed, the sufficiency of the Appellants' Specification is particularly clear for the claims drawn to methods of modifying endosperm in specific plant genera and species. In discussing the adequacy of the Written Description for the claimed methods, the Board states, "the disclosure as filed does not adequately demonstrate possession of the claimed genus

encompassing all partial sequences that act to modify the endosperm of any plant." Board Decision, page 46, lines 12-14. Yet claims 83, 84, 85, 91, 92, and 93 are not broadly directed to any plant. Rather, these claims recite methods in which the *Arabidopsis* Met1 or *Z. mays* Met1 ortholog is introduced into closely-related plants, or plants of the same genus: the *Brassica* genus (of the same family as *Arabidopsis*), a *Brassica napus* plant, *or* a *Z. mays* plant. Here, the Board overlooked the arguments presented in Appellants' Brief at pages 19-20, and also, Example 5 of Appellants' Specification, which discloses the transformation of *Brassica campestris* and *Brassica oleraceae* plants with a partial Met1 sequence (pAGL5Met1as).

Consequently, based on the Specification, the level of skill in the art, and the development of the case law and technology, those skilled in the art would conclude that the Appellants were in possession of sufficient representative species of plants and partial-length oligonucleotides and polynucleotides for claims 20, 21, 62-67, 69, 71, 76-78, and 80-93 at the time of filing. Thus, Appellants request consideration of the full record in keeping with the advances in technology and case law that mandated revision of the U.S.P.T.O.'s Guidelines on oligonucleotides.

4. The Board has overlooked binding Federal Circuit case law.

On page 46, lines 5-8 of the Board's decision, the Board states, "we find with respect to the Written Description rejection…that additional exemplification in the Specification is required to describe modification of endosperm in any plant as claimed." In so stating, the Board has ignored the arguments made in Appellants' Brief at page 12. In particular, Federal Circuit case law expressly holds that examples are not necessary to satisfy the Written Description requirement under 35 U.S.C. § 112, first paragraph.

In *Falko-Gunter Falkner v. Inglis*, the Federal Circuit stated, "Examples Are Not Required…only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation." 448 F.3d 1357, 1366 (Fed. Cir. 2006) (quoting *LizardTech, Inc. v. Earth Resources Mapping, PTY, Inc.* 424 F.3d 1336, 1354 (Fed. Cir. 2005)). Indeed, the court has found that even where claims are drawn to generic inventions, these claims are not unpatentable

merely because working examples have not been provided across the claimed genus. *See Capon v. Eshher*, 418 F.3d 1349, 1360 (Fed. Cir. 2005). Rather, the "certainty required of the disclosure is not greater than that which is reasonable, having due regard to the subject matter involved." *Id.*

Here, the Board has not given due regard to the subject matter involved, particularly given the arguments set forth above regarding the sufficiency of the species present in Appellants' disclosure as it would be understood by those having ordinary skill in the art. Absolute certainty and/or examples demonstrating that each possible oligonucleotide described would work in the claimed methods are not required under the Written Description requirement. Importantly, while Appellants' claims encompass the use of partial fragments, the claims do not allow variation in the nucleotide sequence of these fragments. That is, the nucleotide sequence of *Arabidopsis* Met1 (or the *Z. mays* Met1 ortholog) limits and defines the structure of any effective partial fragments. In addition, as the revised U.S.P.T.O. Guidelines recognize, there are art-recognized correlations between, for example, an antisense oligonucleotide's function and a target mRNA's structure. *See* Example 12, Written Description Training Materials. Accordingly, one having ordinary skill in the art would have recognized that Appellants had possession of the full scope of the claimed invention, in light of the exemplification in the Specification and the understanding of the evolution of this field embraced by the U.S.P.T.O. Guidelines. For at least these reasons, Appellants request reconsideration of the Board's remarks and decision on this point.

Similarly, the Board misinterpreted Federal case law when it articulated the legal standard for Written Description. The Board cites *LizardTech* as establishing that, "while 'examples explicitly covering the full scope of the claim language' typically will not be required, a sufficient number of representative species must be included 'to demonstrate that the patentee possessed the full scope of the [claimed] invention.'" Board Decision at page 44, lines 12-14. Here, the Board has removed the cited language from its context, and word-order, in the opinion and given it a meaning different from that which the court intended. For instance, the Board's interpretation is not reconcilable with the complete language of the section from which the cited phrases were taken:

> [A] recitation of how to make and use the invention across the full breadth of the claim is ordinarily sufficient to demonstrate that the inventor possesses the full scope of the invention, and vice versa....A claim will not be invalidated on section 112 grounds simply because the embodiments of the Specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent Specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the Specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.

Id. at 1345 (internal citations omitted). The holding of *LizardTech* is not that "a sufficient number of representative species" are required to show possession, but that "the Specification [] reasonably convey to a person skilled in the art that [the inventor] had possession of the claimed subject matter at the time of filing'...." *Id.* at 1346 (citation omitted). As explained above, the level of skill in the art of oligonucleotides and the pre-existing knowledge of Met1 and Met1 orthologs in the art were sufficient to convey to a person of ordinary skill in the art that the inventors had possession of the full breadth of the claimed subject matter. Thus, Appellants respectfully request that the Board apply the law in a manner consistent with the updated Guidelines and Federal Circuit case law.

5. Inconsistent statements made by the Board require clarification

On page 47, lines 9-10 and 21-23 of the Board's decision, the Board stated, "the Written Description rejection of claims 83, 84, 91, and 92 is affirmed." However, at page 47, lines 18-19, the Board stated, "the lack of the written description rejection of claims (*except claims 83, 84, 91 and 92*) is affirmed." (Emphasis added.) Appellants request rehearing to resolve the inconsistency between the statements affirming the rejection of all claims and the statement appearing to reverse the rejection claims 83, 84, 91, and 92, under the Written Description requirement.

For at least the above reasons, Appellants respectfully request rehearing of the rejection of claims 20, 21, 62-67, 69, 71, 76-78, and 80-93 under 35 U.S.C. § 112, first paragraph, for lack of Written Description.

B. Enablement

1. The Board has raised a new ground of rejection related to the predictability of the present invention.

On page 39, lines 8-11, the Board states that "the cited references…support a level of unpredictability in the art." In addition, on page 41, lines 11-15 of the Board's decision, the Board states, "we find that the evidence before us shows that down regulation of plant genes often has an effect on one portion of a plant and not other portions of a plant." These statements give rise to a new ground of rejection under 37 C.F.R. 41.50(b). As such, Appellants present new arguments in response under 37 C.F.R. 41.52(a)(3).

The publications cited by the Board as evidence of the alleged unpredictability of the art are not relevant to the predictability of achieving Met1 transgene expression when that expression is targeted to reproductive tissues, as presently claimed. In fact, the cited references disclose only the use of the CaMV 35S constitutive promoter or a vegetative tissue specific promoter. *See, e.g.,* Hibino at page 292, col. 2, Bolitho at Fig. 1, Oliver at Fig. 1, and VanderKrol at Fig. 1, each using the CaMV 35S constitutive promoter; *see also*, Sulehuzzaman, employing a tuber specific promoter. In contrast, the claimed invention targets expression of the Met1 construct (or *Z. mays* Met1 ortholog construct) to the female germ line.

A person of ordinary skill in the art would have appreciated that the use of a promoter that targeted expression to a tissue of interest would eliminate sequelae associated with constitutive expression of a particular oligonucleotide. The inventors' rationale for targeting the female germ line was to avoid such consequences. *See, e.g.,* Example 4 of Appellants' Specification. The inventors sought to "restrict demethylation as much as possible to the germ line or gametes." *Id.* In addition, the inventors desired restriction of imprint removal or attenuation to the male or female gamete to "prevent the attenuation of the interploidy cross effect due to the expression of the hypomethylation gene (Met1as) within the endosperm." *See* Appellants' Specification at page 15, line 22-26. Thus, the inventors themselves provide a

means of predictably modifying endosperm, namely, targeting expression to the female germ line. In light of the focused scope of the claimed subject matter, Appellants request redetermination of the level of predictability in the art for the claimed invention.

2. The Board has overlooked arguments supporting the sufficiency of enablement of claims 63, 69, 76, and 86-93.

The Board overlooked Appellants' analysis of separately-argued claims 63, 69, 76, and 86-93. Here, the Board erred in stating, "Appellant attempts to argue claims 63, 64, 67, 69, 76, and 86-93 separately by simply listing their limitations." On pages 25-27 of Appellants' Brief, however, Appellants explicitly incorporated the arguments presented for claims 21, 64, 66, 77, 82, or 83, for example, into the arguments supporting the patentability of claims 63, 69, 76, and 86-93. The Board conceded that the arguments set forth for claims 21, 64-67, 71, 77, and 79-85 constituted separate arguments under 37 C.F.R. 41.37(c)(1)(vii). *See* Board Decision at pages 41-42. Thus, claims 63, 69, 76, and 86-93 independently stand or fall and Appellants request rehearing on the adequacy of enablement for these claims.

CONCLUSION

For the above-stated reasons, Appellants respectfully request rehearing and vacation of the Board's decision affirming the rejection of claims 20, 21, and 62-67, 69, 71, 76-78, 80-93, and return of the proceeding to the Examiner to issue of a Notice of Allowance.

No fee is believed due. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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